(i) measuring absorbance of radiation by said specimen with said blood substitute interferent present; and

(ii) incorporating said absorbance measured in step b(i) in the following algorithm:

g/L Hb = A(558) - B(570) + C(730) - D

where numbers in the parenthesis are the first derivative of absorbance at the wavelengths (nm) shown, where A, B, C, and D are constants, and calculating the concentration said liberated Hb in said specimen.

18. The method of claim 17 wherein said concentration of liberated Hb is determined in the presence of one or more additional interferents chosen from the group consisting of intralipid (IL), bilirubin (BR) and biliverdin (BV).

Remarks

Please update the USPTO records to indicate the new Attorney Docket Number 01194.002US1.

Claims 1 and 8 are amended herein, no claims are added, and no claims are cancelled. Accordingly, claims 1-18 remain pending in the present application.

Applicant has amended claim 1 to indicate that the method is directed to identifying an interferent within "a specimen in the presence of a blood substitute, one or more other interferents, and at least one analyte...". Support for this amendment can be found in the application, for example, on page 4, lines 7-11, page 18 line 23 to end of page, or page 23, line 20 to page 24 line 6.

Claim 8 has been amended to further clarify the text of the claim.

The amended claims are amended clarify the recitations therein and are not narrowing amendments proposed for reasons relating to patentability as discussed in *Festo v. Shoketsu Kinzoku Kogyo Kabushiki Co.* 72 F.3d 558 (Fed. Cir. 2000). Accordingly, it is intended that the claims are entitled to a full scope of equivalents

Applicant submits that no new matter has been introduced in making these amendments.

Rejections under 35 U.S.C. 112

The Examiner has objected to claims 1-7 under 35 U.S.C. 112 alleging that the claims are indefinite for failing to point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner indicates that in claim 1, an interferent is a relative thing since it interferes with the analysis of another component of a sample, and since there is no analyte in claim 1, the process is either lacking steps relating to the analysis of the analyte or the interferent is actually the analyte for claim 1 and the claims which depend therefrom.

Applicant has amended claim 1 to clarify the language of claims 1-7 and indicate that the concentration of an interferent may be determined in a sample comprising at least one analyte. Applicant submits that this amendment indicates that the method is directed to determining the concentration of an interferent in a specimen comprising an analyte. Support for such a method is found in the specification, for example, on page 4, lines 7-11, and page 5, lines 5-9, where the effect of an interferent is corrected for during the measurement of an analyte. However, it is to be understood that the concentration of an interferent may also be determined (e.g. page 4, lines17-29, and elsewhere) following the methods described herein.

Based on the amendment made to claim 1 and that claims 2-7 defend from claim 1, Applicant asserts that the subject matter of claims 1-7 is definite, clear and unambiguous. Removal of the rejection to claims 1-7 under 35 U.S.C. 112 is requested.

Reservation of the Right to Swear Behind References

Applicant maintains its right to swear behind any references which are cited in a rejection under 35 U.S.C. §§102(a), 102(e), 103/102(a), and 103/102(e). Statements distinguishing the claimed subject matter over the cited references are not to be interpreted as admissions that the references are prior art.

Rejections under 35 U.S.C. 102 (b), (e)

The Examiner has rejected to claim 1 under 35 U.S.C. 102(b) or (e) in view of each of Chai, Fitch, Golden, Hamilton, Lin, Pascual-Marti, Phillips, Randall, Sagusa, Stimmel and Vink.

Applicant has amended claim 1 so that claim 1 now claims a method of identifying the presence of a selected interferent contained in a specimen in the presence of a "blood substitute".

Applicant submits that none of the references cited by the Examiner disclose nor suggest a method of identifying the presence of a selected interferent in the presence of a blood substitute.

Chai teaches determination of bilirubin by three wavelength spectrophotometry. Chai does not teach a method of identifying the presence of a selected interferent contained in a specimen in the presence of a blood substitute and one or more other interferents, nor does Chai suggest that the method may be employed to identify the presence of a selected interferent in a specimen in the presence of a blood substitute. Thus, Applicant argues that amended claim 1 is not anticipated by Chai.

Fitch teaches measurement of urinary 3-methylhistidine with cationic-exchange resin. Fitch does not disclose a method of identifying the presence of a selected interferent contained in a specimen in the presence of a blood substitute and one or more other interferents as recited in amended claim 1 of the instant application. Further, since Fitch pertains only to the measurement of specific compounds in urine, Applicant asserts that the cited reference does not anticipate a method of identifying the presence of a selected interferent contained in a specimen in the presence of a blood substitute and one or more other interferents. Applicant submits that amended claim 1 of the present application is not anticipated by Fitch.

Golden discloses the quantitative determination of bilirubin in urine. There is no disclosure or suggestion in Golden of a method of identifying the presence of a selected interferent contained in a specimen in the presence of a blood substitute and one or more other interferents. Since no discussion of blood substitutes or blood samples is disclosed in Golden, Applicant asserts that Golden does not anticipate amended claim 1 of this invention.

Hamilton discloses a spectrophotometric method for the determination of Evans blue dye in the presence of haemolysis and turbidity. Hamilton does not disclose a method of identifying the presence of a selected interferent contained in a specimen in the presence of a blood substitute and one or more other interferents. Applicant asserts that Hamilton does not anticipate amended claim 1 of the instant invention.

Lin teaches a correction method for ultraviolet spectrophotometry of turbid systems. The method may be employed in a determination of N-polyethoxylated alkyl amide in clay supernatant. There is no disclosure or suggestion of a method of identifying the presence of a selected interferent contained in a specimen in the presence of a blood substitute and one or more

other interferents, as claimed in amended claim 1 of the instant application. Further, there is no suggestion that the method disclosed by Lin could be employed to identify the presence of a selected interferent contained in a specimen in the presence of a blood substitute. Applicant submits that Lin does not anticipate claim 1.

Pascuel-Marti discloses a theoretical and experimental study extending the application of the linear absorbance method to complex systems which present two spectral interferences. The theoretical equations developed are experimentally tested by determination of methal orange in the presence of methyl red and cresol red. Further, the influence of the variables involved in the linear absorbance method is studied. The Pascuel-Marti reference does not disclose a method of identifying the presence of a selected interferent contained in a specimen in the presence of a blood substitute and one or more other interferents. Thus, Applicant asserts that the Pascuel-Marti reference does not anticipate amended claim 1 of the instant application.

Phillips teaches a method for determining the presence of an analyte in a fluid. The method involves taking a reflectance reading from one surface of an inert porous matrix impregnated with a reagent that will interact with an analyte to produce a light absorbing reaction product when the fluid being analysed is applied to another surface and migrates through the matrix to the surface being read. Reflectance measurements are made at two separate wavelengths in order to eliminate interferences. The Phillips document does not disclose a method of identifying the presence of a selected interferent contained in a specimen in the presence of a blood substitute and one or more other interferents. Applicant also wishes to inform Examiner that the Phillips reference relates to taking reflectance readings and not measuring the absorbance of radiation by the selected interferent in the specimen as is claimed in step ii) of claim 1 of the instant application. Applicant argues that the Phillips reference does not anticipate claim 1 of the present application.

Randall discloses interference by haemolysis, icterus and lipaemia in assays on Beckman Synchron CX5 instruments and methods for correction. The Randall article does not disclose a method of identifying the presence of a selected interferent contained in a specimen in the presence of a blood substitute and one or more other interferents. Thus Applicant argues that Randall does not anticipate claim 1.

The Sagusa patent discloses adding a color former to blood serum samples and measuring specific components based on the light absorbance caused by the coloring. For one sample, a differential light absorbance between two wavelengths and each of a long wavelength region, middle wavelength region and short wavelength region within a visible wavelength band is determined. The degree of chyle is determined from the measurements for the long wavelength region, the degree of haemolysis is determined form the measurements for the middle wavelength region, and the degree of icterus is determined from the measurements for the short wavelength region. The measurements for the specific components are then corrected by the degree of chyle, the degree of haemolysis and the degree of icterus to obtain highly correct measurements. The patent does not disclose a method of identifying the presence of a selected interferent contained in a specimen in the presence of a blood substitute and one or more other interferents. Applicant argues that Sagusa does not anticipate claim 1.

Stimmel discloses the utilization of a color correction equation with the Kobe reagent for the estimation of estrogens in human urine with low estrogen content. There is no disclosure or suggestion in Stimmel of a method of identifying the presence of a selected interferent contained in a specimen in the presence of a blood substitute and one or more other interferents. Further, since the Stimmel article pertains only to urine, a person of skill in the art would not even be led to employ the disclosure of Stimmel to identify the presence of a selected interferent contained in a specimen as disclosed claim 1 of the instant invention. Based on the differences between the Stimmel reference and claim 1 of the instant invention, Applicant submits that Stimmel does not anticipate claim 1 of the instant application.

Vink discloses a direct spectrophotometric method for determination of bilirubin in the serum of newborns, using a caffeine reagent. There is no suggestion in Vink to a method of identifying the presence of a selected interferent contained in a specimen in the presence of a blood substitute and one or more other interferents as recited in claim 1 of the instant application. Applicant argues that Vink does not anticipate claim 1.

Applicant therefore requests that the rejection against claim 1 of this application under 35 U.S.C. 35 102 (b),(e) be removed.

Rejections under 35 U.S.C. 103(a)

Claims 2-18 have been rejected to under 35 U.S.C. 103(a) with consideration of Sagusa in view of Christenson, Leissing or Mullins and Simon. Applicant respectfully traverses Examiner's rejection.

Christenson discloses that a Hb substitute (Hb_{sub}) may interfere with a number of routine chemical test assays. The hemoglobin substitute was determined to be acceptable at certain concentrations and unacceptable at others for specific assays. However, no methods are disclosed which may be used to identify, quantify or correct for the presence of a selected interferent contained in a specimen in the presence of a blood substitute and one or more other interferents.

Leissing discloses that various haemoglobin solutions are being developed for use as oxygen carrying resuscitation fluids, and that haemoglobin at concentrations as low as 100 mg/dL can cause interference in clinical methods. No specific methods for identifying, quantifying or correcting for the presence of a selected interferent contained in a sample in the presence of one or more other interferents using a spectrophotometer are disclosed or suggested.

Mullins discusses the effects of artificial blood (Fluosol-DA) on clinical chemistry tests and instruments. A 20% emulsion was added to blood specimens in amounts corresponding to the replacement of in-vivo plasma volumes of 10%-50%. The presence of Fluosol interfered to various degrees with specific analytical tests. While the Mullins reference teaches that artificial blood substitutes may alter results of clinical tests, the reference does not teach or suggest a method of identifying, quantifying or correcting for the presence of a selected interferent contained in a specimen in the presence of a blood substitute and one or more other interferents.

Simon discloses that intravenous iron-dextran therapy can cause a red-brown discoloration of the plasma, simulating a hemolytic transfusion reaction. Simon also teaches a rapid and simple test to differentiate between true hemolysis and plasma discoloration due to circulating iron dextran complexes. Simon does not disclose nor suggest a method of identifying, quantifying or correcting for the presence of a selected interferent contained in a specimen in the presence of a blood substitute and one or more other interferents. Further the Simon reference pertains to visual analysis of plasma and there is no disclosure or suggestion that the method is performed using a spectrophotometer as indicated by the claims of the present invention.

Leissing, Christenson, Mullins and Simon each teach that blood substitutes may alter results of clinical tests. However there is no disclosure or suggestion in any of these references to a method of identifying the presence of a selected interferent contained in a specimen in the presence of a blood substitute and one or more other interferents. Rather, these documents disclose one of the problems in the art, i.e. that blood substitutes may alter results, that the present invention is directed to solving.

The Sagusa patent teaches that disturbing materials such as chyle (turbidity), hemolysis (hemoglobin) and icterus (bilirubin) may interfere with the analysis of an analyte, and that an ultraviolet detectible compound may be added to a sample for the detection of these disturbing materials. For example, in Col. 3, line 34 - Col. 4, line 12, it is stated that:

> Among others, when the absorption by the test sample is superimposed on those absorption spectra [the absorption spectra for the disturbing chromogens such as chyle, hemolysis and icterus], the analysis thereof is more difficult, and even if it is possible, the precision is materially low. Therefore where many items are to be simultaneously tested for the same test sample..., it is easier to analyse a spectrum for an item which is most easy to analyse, determine the amounts of the three disturbing materials from the resulting spectrum and correct the measurements for other items using the disturbing amounts of the disturbing materials....The items which are most easy to analyse the disturbing chromogens are those items which are measured using ultraviolet absorption, such as glutamic acid-oxiaroacetic-transaminase (GOT), glutamic acid-pyrunic acid-transaminase (GPT), lactic acid ...In the measurement of those test items, the light absorption of the test sample...occurs only in the ultraviolet region, and in the visible region, it does not overlap the absorption spectrum of the disturbing material [turbidity, hemolysis and icterus]...By analysing the spectra of the reactant in the visible wavelength region in the GOT measurements, the amounts of disturbing chromogens can be determined.

In column 6, lines 24-30 it is stated:

> While the spectrum for the GOT measuring liquid is used in the above embodiment to determine the amounts of disturbing chromogens, spectra for ultraviolet measurement liquids such as GPT, LDH or HBDH may be used to determine the amounts of the disturbing chromogens.

Applicant submits that the combined teachings of Sagusa, Leissing, Christenson, Mullins, and Simon suggest to one of skill in the art that an ultraviolet color former be added to a blood sample which comprises a blood substitute to determine the amount of turbidity, hemoglobin and bilirubin in a sample. However, no color former addition to blood samples is contemplated by the present invention.

Further, there is no direction or suggestion in Sagusa, Leissing, Christenson, Mullins, and Simon that would direct a person of skill in the art to a method for identifying the presence of a selected interferent contained in a specimen in the presence of a blood substitute and one or more interferents using a method of correcting for the concentration of a blood substitute in a specimen, as claimed in claims 1-7, a method to measure analyte concentration obtained from a specimen, as described in claims 8-16, or a method of distinguishing true hemolysis from pseudo hemolysis caused by a blood substitute as described in claims 17 and 18.

Based on the teachings of Sagusa in view of Leissing, Christenson, Mullins, and Simon, Applicant submits that a person of skill in the art would not be led to the subject matter as claimed in claims 2-18 of the instant application. Applicant requests that the rejection of claims 2-18 under 35 U.S.C. 103(a) be removed.

Conclusion

Early and favourable prosecution of this application on its merits is respectfully requested. The Examiner is invited to telephone Applicant's attorney (612-349-9587) to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Seice with sufficient postage as first class mail, in an envelope addressed to: Commissioner of Patents, Washington, D.C. 20231, on this 5th day of November, 2001.

Candis B. Buending
Name

_____
Signature